

A clean version of each replacement claim is submitted below. Please enter each claim.

- 1) (Amended) A process for delivering a nucleic acid to a cell, comprising:
- a) forming a complex consisting of a nucleic acid and a polymer in a solution wherein the complex has a net charge less negative than the nucleic acid;
  - b) ionically attaching a charged polymer to the complex of step a) in sufficient amount to form a new complex having a net charge more negative than the complex in step a);
  - c) inserting the complex into a mammal;
  - d) delivering the complex to the cell.
- 3) (Amended) The process of claim 1 wherein the polymer is selected from the group consisting of PLL and PEI.
- 8) (Amended) A complex for delivering a nucleic acid to a cell, comprising:
- a) the nucleic acid;
  - b) a polycation polymer complexed with the nucleic acid; and,
  - c) a polyanion polymer, having a molecular weight of at least 30 kDa, complexed with the polycation.

### REMARKS

#### Rejection of claims under of 35 U.S.C. 112:

Claim 13 has been rejected under the first paragraph of §112 for no literal support in the Specification. Applicants regret omitting to point to page 7, lines 11-16 as the support for the amendment. The specification reads: "The polymer can be a homopolymer in which a single monomer is used or can be copolymer in which two or more monomers are used. Types of copolymers include alternating, random, block and graft." The polyanionic polymer and the polycationic polymer are each monomers of the copolymer.

Claims 2, 3, and 17 have been rejected under §112.

Claim 2 has been cancelled and claim 3 has been amended to recite a "polyion" in place of "polycation" to remove the confusion regarding negative charge.

Claim 17 is dependent from claims 16 and 15. However, none of the claims 15-17 recite language about the 'complex having a net charge which is less negative than the charge of the nucleic acid' as stated in the Action. Therefore, the rejection is believed to be without basis.

Claims 1-7 and 15-18 have been rejected under §112 second paragraph for being indefinite.

Independent claim 1 has been amended according to the Examiner's suggested language.

The Action states that claim 17 requires that "the polymer" be selected from a selected group. However, claim 16 actually states that "the polycation" be selected from PLL and PEI. Claim 17 requires a "negatively charged polyion" and does not use the term 'polymer.' Independent claim 15 recites: "a polycation non-covalently attached to a polyanion; complexed with, a negatively charged polyion." The terminology is used to identify each component of the complex: 1) a polycation; 2) a polyanion; and 3) a negatively charged polyion. The negatively charged polyion is really a second polyanion.

The format "consisting of" is used in claim 17 because the polycation is a polymer, however, it is also a monomer when attached to the polyanion which is also a polymer and a monomer. The "consisting of" language refers to the monomer-polymers individually, not the polymer which results from the attachment of two individual monomer-polymers. Therefore, claims 15-17 are believed to be definite under the meaning of §112.

The rejections are believed to be obviated.

Rejection of claims under 35 U.S.C. 102:

Claims 8, 10, 12, 14-16 and 18 are rejected under §102(b) as being anticipated by Erbacher et al. Applicants respectfully disagree.

Applicants claim 8 recites an ionic complex. In contrast, Erbacher teaches PLL having biotin covalently bound. Such a covalent attachment does not anticipate an ionic, reversible connection as recited by Applicants.

Claims 8, 10, 12, 14-16 and 18 are rejected under §102(b) as being anticipated by Plank et al. Applicants have amended the claims to obviate the rejection.

The Plank et al. reference teaches peptides of, at most, 4 kDa. The peptides used have known membranolytic activity.

Amended claim 8 now recites "a polyanion polymer, having a molecular weight of at least 30 kDa, complexed with the polycation." Support for the amendment may be found in the Specification beginning in Example 1 on page 22, line 25. Applicants believe that the amendment to claim 8 obviates the rejection.

Claims 8, 10, 12, 14-16 and 18 are rejected under §102(b) as being anticipated by Gao et al. or Kupfer et al. Applicants respectfully disagree.

Both Gao and Kupfer teach covalently bound polyanions or polyanions bound via a streptavidin-biotin interaction. Conversely, Applicants disclose polyanions and polycations having ionic interactions. Therefore, the two references do not anticipate Applicants claims.

Claims 8, 10, 12, 14-16 and 18 are rejected under §102(b) as being anticipated by Boussif et al. Applicants respectfully disagree.

Boussif teaches a binary complex. Applicants are claiming a tertiary complex, therefore, Boussif does not anticipate their claims.

Claims 8, 10, 12, 14-16 and 18 are rejected under §102(b) as being anticipated by Kabanov et al. Applicants respectfully disagree.

Kabanov teaches a binary complex not a tertiary complex as in Applicants' claims. Therefore, the claims are not anticipated.

Claims 8, 10, 12, 14-16 and 18 are rejected under §102(b) as being anticipated by Baker et al. Applicants respectfully disagree.

Baker teaches adenovirus linked to the polycation by a streptavidin-biotin linkage, not an ionic interaction as disclosed by Applicants. Therefore, the Baker art does not anticipate Applicants' claims.

Claims 8, 10, 12, 14-16 and 18 are rejected under §102(b) as being anticipated by Katayose et al. Applicants respectfully disagree.

Katayose teach forming an intermediary complex that is not stable and could not be used for delivering a nucleic acid to a cell. In contrast, Applicants complex is used for delivering nucleic acids to cells as claimed. Therefore, the Katayose prior art does not anticipate Applicants' claims.

#### Response to Arguments:

Applicants acknowledge the Examiner's statements on page 9 of the Action. Applicants believe that the Declaration of James E. Hagstrom regarding histones complexed with DNA indicates the conception of the invention. Although all of the species disclosed in the specification were not shown in the Declaration, histone is one species of polycation that is representative of the others. Applicants have used various polycations in their current description however histone was the first polycation tried and therefore deserves broader consideration as a representative polycation.

#### Rejection of claims under 35 U.S.C. 103:

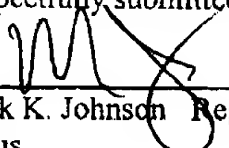
Claims 1, and 4-7 have been rejected under §103 as being obvious from reading Gao or Kupfer.

Applicants have amended claim 1 to recite "ionically attaching" a polymer. The cited references describe either covalent, streptavidin-biotin, or antibody interactions as opposed to ionic interactions.

Applicants believe the amendment obviates the rejection.

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendments and discussion, it is submitted that claims 1-8, 10, 12-19 should be in condition for allowance and Applicants respectfully request an early notice to such effect.

Respectfully submitted,

  
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I hereby certify that this correspondence is being sent by facsimile transmission to fax # 703.305.3014 in art unit 1632 and is addressed to: Assistant Commissioner for Patents, Washington, DC 20231 on Friday, February 14, 2003.

  
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Signature